

acid and/or uronic acid derivatives) to a heating treatment at 30-400 degrees C for from a few seconds to a few days:

(e) pentose:

(f) pentose derivatives:

(g) compounds containing pentose:

(h) compounds containing pentose derivatives: and

(2) purifying the substance having an apoptosis-inducing ability from the heat-treated compound.

11. (Amended) An apoptosis-inducing compound selected from

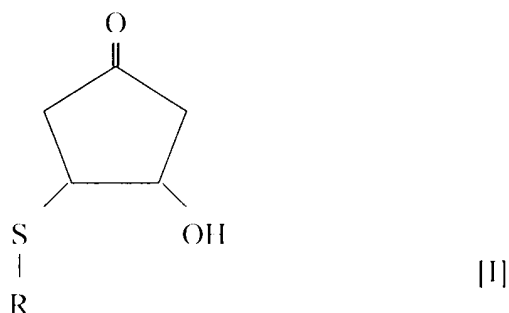
4-(9-adeninyl)-2-cyclopenten-1-one,

4-(9-guaninyl)-2-cyclopenten-1-one,

1,5-epoxy-1-hydroxy-3-penten-2-one,

2-(3,4-dihydroxy-1-butenyl)-4-(2-formylvinyl)-1,3-dioxolane, and

the compound represented by the following formula [I]



(In the formula, R is a residual group after removal of an SH group from [a compound] an amino acid containing an SH group or a peptide containing an amino acid containing an SH group.)

12. (Amended) A pharmaceutical agent for therapy [or prevention] of a disease [having a sensitivity to a compound] selected from the group consisting of cancer,

response, autoimmune disease, inflammation, arthritis, rheumatic arthritis, inflammatory intestine diseases, insufficiency of blood vessel function, etiological dilation of blood vessel, damage of tissues, cardiovascular ischemia, sensitivity to pain, cerebral ischemia, diseases caused by angiogenesis and viral diseases, characterized in that, said pharmaceutical agent contains a compound selected from

4,5-dihydroxy-2-pentenal,

4-hydroxy-2-cyclopenten-1-one,

4-(9-adeninyl)-2-cyclopenten-1-one,

4-(9-guaninyl)-2-cyclopenten-1-one,

2-(3,4-dihydroxy-1-butenyl)-4-(2-formylvinyl)-1,3-dioxolane,

1,5-epoxy-1-hydroxy-3-penten-2-one, and

a compound represented by the formula [ I ]

characterized in that, said pharmaceutical agent contains a compound selected from

4,5-dihydroxy-2-pentenal,

4-hydroxy-2-cyclopenten-1-one,

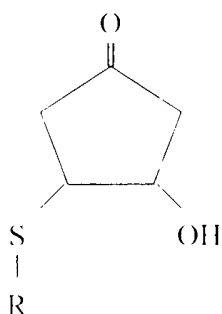
4-(9-adeninyl)-2-cyclopenten-1-one,

4-(9-guaninyl)-2-cyclopenten-1-one,

2-(3,4-dihydroxy-1-butenyl)-4-(2-formylvinyl)-1,3-dioxolane,

1,5-epoxy-1-hydroxy-3-penten-2-one, and

a compound represented by the formula [ I ] as an effective component



[ I ]

(In the formula, R is a residual group after removal of an SH group from [a compound] an amino acid containing an SH group or a peptide containing an amino acid containing an SH group).

Please cancel claims 13 and 15.

#### Remarks

Applicant has amended claims 1, 11 and 12.

(1) The Office Action rejected claim 12 asserting that it would take an undue amount of experimentation to determine for the treatment of which specific diseases the claimed agents are useful, and that there is a good reason to doubt that the claimed compounds are useful in prevention of disease. In response thereto, applicant has deleted the description "or prevention" from claim 12 and has amended claim 12 so that the claimed pharmaceutical agent is for therapy of enumerated diseases, as set forth in the specification.

The diseases are supported by the specification as follows:

As to cancer, page 19.

As to rheumatism, page 22.

As to diabetes mellitus and dwarfism, page 24.

As to systemic hypotension, lowering in blood pressure response, autoinimmune disease, inflammation, arthritis, rheumatic arthritis, inflammatory intestine diseases, insufficiency of blood vessel function, etiological dilation of blood vessel, damage of tissues, cardiovascular ischemia, sensitivity to pain, cerebral ischemia, and diseases caused by angiogenesis, page 28.

As to viral diseases, page 31.

(2) The Office Action rejected claims 1-9 and 25 asserting that the structure of the final product (which results from the heating treatment) is not clear. Also, claims 1-10 and

forth. Further, claims 1-10 and 14-24 were rejected on the assertion that it is not clear what specific compound was heated in order to produce what specific final product.

In response to these rejections, the following points are pertinent: The present invention is based on the finding that heating pentose, pentose derivatives or compounds containing them leads to the production of a substance having an apoptosis-inducing ability in the heat-treated compound. There is no limitation as to the compound to be used as a raw material. Also, the substance having an apoptosis-inducing ability that is produced in the heat-treated compound is not necessarily only one compound. That is, the present invention is not restricted to a specific substance having an apoptosis-inducing ability.

As to the rejection that no condition of the heating process has been set forth, claim 1 has been amended to specify the condition of the heating process based on the description in lines 2-3, page 12 of the specification. Thus, the above rejection is overcome.

(3) The Office Action pointed out that in claim 12 it is not clear what is encompassed by the variable "R."

In response thereto, claims 11 and 12 have been refined to point out that "R" is "a residual group after removal of an SH group from an amino acid containing an SH group or a peptide containing an amino acid containing an SH group." This definition is supported by page 38 of the specification.

(4) The Office Action asserted that claims 12 and 13 as well as claims 14 and 15 are substantial duplicates. In response thereto, claims 13 and 15 have been deleted.

(5) The Office Action pointed out that it is not clear what compounds are encompassed by the food or beverage claims 14-15. As mentioned in above (2), the present invention is not restricted to a specific substance having an apoptosis-inducing ability. The

process contains a substance having an apoptosis inducing ability. Thus, for those skilled in the art, it is apparent that food or beverage containing the above heat-treated compound is capable of exhibiting an apoptosis-inducing ability.

(6) The Office Action rejected claims 1-10 and 16-25 are anticipated by or obvious from the disclosure of U.S. Patent 5,015,296 to Dobler et al or U.S. Patent 5,792,868 to Izawa et al.

Dobler et al disclose a process for preparing an epimer by heating a pentose or hexose. Izawa et al disclose a process for producing an acyclic nucleoside by heating ribonucleoside. Neither reference discloses that the heating -treatment product has an apoptosis- inducing ability.

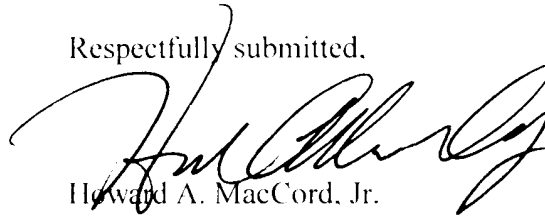
Claim 1 has been amended to include a step of purifying the substance having an apoptosis-inducing ability in addition to a step of heating treatment. By such amendment, it is clear that the inventions of claims 1-10 and 16-25 are neither anticipated by nor obvious over Dobler et al or Izawa et al.

(7) The Office Action rejected claims 11-15 are anticipated by or obvious from the disclosures of U.S. Patent 6,184,381 B1 to Ikariya et al or U.S. Patent 5,984,882 to Rosenschein et al. Ikariya et al disclose 4-hydroxy- 2-cyclopenten- 1-one, but they do not disclose the physiological activity thereof. In particular, they do not disclose that the above compound has an apoptosis-inducing ability. Rosenschein et al disclose combining the use of antioxidant such as N-acetylcystein or glutathione and the induction of apoptosis using ultrasound. On the contrary, the present invention is not characterized by the use of the above antioxidant. The compound used in the present invention has different structure from that of the above antioxidant.

None of the cited references disclose that the compound disclosed in the present invention has an apoptosis-inducing ability. Therefore, claims 11-15 are neither anticipated by

The Applicant submits that by this amendment he has placed the case in condition for immediate allowance and such action is respectfully requested. However, if any issue remains unresolved, Applicant's attorney would welcome the opportunity for a telephone interview to expedite allowance and issue.

Respectfully submitted,



Howard A. MacCord, Jr.  
Registration No. 28,639  
MacCord Mason PLLC  
P. O. Box 2974  
Greensboro, NC 27402  
(336) 273-4422

Date: 4 February 2003  
File No.: 4629-006

CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS DOCUMENT IS  
BEING DEPOSITED WITH THE UNITED STATES  
POSTAL SERVICE AS FIRST-CLASS MAIL, IN AN  
ENVELOPE ADDRESSED TO **COMMISSIONER  
FOR PATENTS, WASHINGTON, D.C. 20231**

ON 4 February 2003

(Date of Deposit)

Christian E. Carter

\_\_\_\_\_  
Name of Depositor

  
\_\_\_\_\_  
Signature